

PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Article 36 and Rule 70)

REC'D 14 FEB 2005

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Applicant's or agent's file reference UNI-003-PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP 03/14567	International filing date (day/month/year) 18.12.2003	Priority date (day/month/year) 18.12.2002
International Patent Classification (IPC) or both national classification and IPC C07J7/00		
Applicant UNIBIOSCREEN S.A.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).
- These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the opinion
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 14.07.2004	Date of completion of this report 10.02.2005
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Wörth, C Telephone No. +49 89 2399-8726 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP 03/14567

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-72 as originally filed

Claims, Numbers

1-20 as originally filed

Drawings, Sheets

1/4-4/4 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
 - ☐ the language of publication of the international application (under Rule 48.3(b)).
 - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- ☐ contained in the international application in written form.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority in written form.
 - ☐ furnished subsequently to this Authority in computer readable form.
 - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
 - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 20 with respect to IA

because:

☒ the said international application, or the said claims Nos. 20 with respect to IA relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-20
	No: Claims	
Inventive step (IS)	Yes: Claims	1-20
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-19
	No: Claims	

2. Citations and explanations

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. **PCT/EP 03/14567**

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP 03/14567

1. Re Item I (*Basis of the report*)

Reference is made to the following documents:

- D1: MODI, SANDEEP P. ET AL: "Conjugate addition of Grignard reagents to enones and dienones" JOURNAL OF ORGANIC CHEMISTRY (1989), 54(10), 2317-21, XP002242748
- D2: CIOBANU, L. C. ET AL: "Synthesis and steroid sulfatase inhibitory activity of C19- and C21-steroidal derivatives bearing a benzyl-inhibiting group" EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY (2001), 36(7-8), 659-671, XP004372876
- D3: R. P. BOIVIN ET AL.: "Structure-Activity Relationship of 17alpha-Derivatives of Estradiol as Inhibitors of Steroid Sulfatase" J. MED. CHEM., vol. 43, 2000, pages 4465-4478, XP002232869
- D4: ENDO, YASUYUKI ET AL: "Oxygenated cholesterol as ligands for cytosolic-nuclear tumor promoter binding protein: Yakkasteroids" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS (1993), 194(3), 1529-35, XP002232867
- D5: JP 06 321782 A (SHUDO KOICHI, JAPAN) 22 November 1994 (1994-11-22)
- D6: BERGSTROM, CARL P. ET AL: "Inhibition of cholesterol side-chain cleavage. Part 5. Synthesis of 22-(p-chlorophenyl)cholesterol analogs" DRUG DESIGN AND DELIVERY (1991), 7(4), 259-68, XP001079777

2. Re Item III (*Non-establishment of opinion with regard to novelty, inventive step and industrial applicability*)

Claim 20 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

3. Re Item V (*Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement*)

3.1 Novelty

The subject-matter of the present application differs from

- D1 in view of the **proviso** at the end of present claim 1 excluding compound 7c of D1

- D2-D6 in view of the **benzyl-like substitution at position 16** of the steroid skeleton.

The requirements of novelty are fulfilled.

3.2 Inventive step

At present, document D2 is considered as **closest prior art**. This document discloses C19 and C21 steroidal derivatives bearing a benzyl-group having inhibitory activity on steroid sulphatase (see section conclusions, page 664) being consequently useful in the treatment of hormone sensitive cancers (see abstract).

In view of this document, the **problem to be solved** can be regarded as the provision of further compounds having the same biological activity as those in D2.

The **solution** consists in compounds of formula IB. In view of example 3, table D and E, the problem is at present considered as solved at least for one compound claimed.

However, the solution is considered as **obvious** in the light of the combined technical teaching of documents D2 and D3. Document D3 teaches the introduction of a benzyl **at position 16 of a steroid skeleton (see scheme 3, compounds 27 and 28 and table 4) in order to achieve the desired biological activity**.

Accordingly, the provision of compounds of formula IB of the present application characterized by a different steroid skeleton and a variable linker (see definition of present "n") is an obvious design possibility for the skilled person having knowledge of the teaching of D2 and D3 in order to solve the problem posed.

However, document D3 teaches away from the presently provided solution by stating that the 17a-position is preferable to position 16 with regard to the inhibition of steroid sulfatase (see D3, page 4470, second paragraph). Furthermore, the presently claimed subject-matter provides additional advantageous activities not mentioned or suggested in the prior art. Example 4 of the present application indicates an anti-migratory effect on cancer cells relevant for the treatment of scar tissue and wounds. This effect is presently considered as being unexpected indicating an inventive step for the claimed subject-matter.

The requirements of inventive step are fulfilled.

3.3 Industrial applicability

For the assessment of the present claim 20 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.